

What is claimed is:

1. A method of identifying oligonucleotide sequence motifs which are correlated with antisense oligonucleotide activity
5 comprising:
 - a. providing a set of antisense oligonucleotide sequences, each of which has an experimentally determined capacity to inhibit expression of its complementary nucleic acid target;
 - 10 b. subdividing each of said antisense oligonucleotide sequences into subsequences of defined length, each unique subsequence being a motif;
 - c. determining which motifs significantly correlate with antisense oligonucleotide activity; and
 - 15 d. eliminating the motifs whose correlation with antisense oligonucleotide activity is unique to a particular nucleic acid target.
2. The method of claim 1 wherein the defined length of the motifs is from two to ten nucleotides in length.
- 20 3. The method of claim 2 wherein the defined length of the motifs is from three to four nucleotides in length.
4. The method of claim 1 wherein determining which motifs significantly correlate with antisense oligonucleotide activity is done by T-test.
- 25 5. The method of claim 1 further comprising relating the probability of antisense oligonucleotide activity to the motif content of each oligonucleotide.
6. The method of claim 5 wherein relating the probability of antisense oligonucleotide activity to the motif content of

each oligonucleotide is done by creation of a logistic regression model.

7. The method of claim 5 further comprising selecting and eliminating motifs that are below a desired threshold of
5 significance for probability of antisense oligonucleotide activity.

8. The method of claim 7 wherein selecting and eliminating motifs that are below a desired threshold of significance for probability of antisense oligonucleotide activity is done
10 using the likelihood ratio test.

9. A method of identifying oligonucleotide sequence motifs which are predictive of antisense oligonucleotide activity comprising:

a. providing a set of antisense oligonucleotide
15 sequences, each of which has an experimentally determined capacity to inhibit expression of its complementary nucleic acid target;

b. subdividing each of said antisense oligonucleotide sequences into subsequences of defined length, each unique
20 subsequence being a motif;

c. determining which motifs significantly correlate with antisense oligonucleotide activity;

d. eliminating the motifs whose correlation with antisense oligonucleotide activity is unique to a particular
25 nucleic acid target;

e. relating the probability of antisense oligonucleotide activity to the motif content of each oligonucleotide;

f. selecting and eliminating motifs that are below a desired threshold of significance for probability of antisense
30 oligonucleotide activity; wherein the remaining motifs are predictive of antisense oligonucleotide activity.

10. The method of claim 9 wherein the defined length of the motifs is from two to ten nucleotides in length.

11. The method of claim 10 wherein the defined length of the motifs is from three to four nucleotides in length.

5 12. The method of claim 9 wherein determining which motifs significantly correlate with antisense oligonucleotide activity is by T-test.

13. The method of claim 9 wherein relating the probability of antisense oligonucleotide activity to the motif content of
10 each oligonucleotide is done by creation of a logistic regression model.

14. The method of claim 9 wherein selecting and eliminating motifs that are below a desired threshold of significance for probability of antisense oligonucleotide activity is done
15 using the likelihood ratio test.

15. An oligonucleotide sequence motif identified according to the method of claim 1.

16. An oligonucleotide sequence motif identified according to the method of claim 9.

20 17. A method of selecting effective antisense oligonucleotide sequences for inhibition of expression of a preselected target nucleic acid comprising:

providing a set of antisense oligonucleotide sequences of a
selected length which are complementary to a preselected
25 target nucleic acid sequence;

selecting the antisense oligonucleotide sequences in the set
which contain at least one activity-enhancing
oligonucleotide sequence motif.

18. The method of claim 17 further comprising selecting the antisense oligonucleotide sequences identified in (b.) which do not contain an activity-decreasing oligonucleotide sequence motif.

5 19. The method of claim 17 further comprising selecting the antisense oligonucleotide sequences identified in (b.) which contain more than one activity-enhancing oligonucleotide sequence motif.

20. A method of selecting effective antisense target
10 sequences for inhibition of expression of a preselected target nucleic acid comprising:

dividing a target nucleic acid sequence into a set of target
sequence regions of a selected length for antisense
targeting;

15 selecting the target sequence regions in the set which contain
at least one activity-enhancing target sequence motif.

21. The method of claim 20 further comprising selecting the target sequence regions identified in (b.) which do not contain an activity-decreasing target sequence motif.

20 22. The method of claim 20 further comprising selecting the target sequence regions identified in (b.) which contain more than one activity-enhancing target sequence motif.

23. An antisense oligonucleotide sequence selected according to the method of claim 17.

25 24. An antisense target sequence selected according to the method of claim 20.

25. A method of designing an antisense oligonucleotide with enhanced likelihood of inhibiting expression of a preselected nucleic acid target comprising targeting said antisense oligonucleotide to a nucleic acid target sequence comprising
5 one or more activity-enhancing target sequence motifs.

26. The method of claim 25 wherein the target sequence does not contain an activity-decreasing target sequence motif.

27. The method of claim 25 wherein the target sequence comprises two or more activity enhancing motifs.

10 28. A method of designing an antisense oligonucleotide with enhanced likelihood of inhibiting expression of a preselected nucleic acid target comprising targeting said antisense oligonucleotide to a nucleic acid target sequence which does not contain an activity-decreasing target sequence motif.

15 29. The method of claim 28 wherein the target sequence contains one or more activity-enhancing target sequence motifs.

30. An antisense oligonucleotide designed according to the method of claim 25.

20 31. An antisense oligonucleotide designed according to the method of claim 28.